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EXPERIMENTAL ARTICLES

In vitro Antifungal Activity of Metal Complexes of a Quaternized Chitosan Derivative with Copper Ions

A. V. Il'ina[a], B. Ts. Shagdarova[a, *], A. P. Lun'kov[a, b], S. N. Kulikov[c, d], and V. P. Varlamov[a]

[a] *Institute of Bioengineering, Research Center of Biotechnology Russian Academy of Sciences, Moscow, Russia*
[b] *Dmitry Mendeleev University of Chemical Technology of Russia, Moscow, Russia*
[c] *Kazan Research Institute of Microbiology and Epidemiology, Kazan, Russia*
[d] *Kazan Federal University, Kazan, Russia*
**e-mail: shagdarova.bal@gmail.com*

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Abstract—Antifungal activity of synthetic metal complexes of quaternized N-(propyl) chitosan derivatives with Cu(II) against yeastlike (*Saccharomyces cereviseae, Rodothorula rubra,* and *Candida albicans*) and mycelial fungi (*Fusarium oxysporum, Alternaria alternata, Cladosporium herbarum*) was studied. In vitro application (at 250–500 μg/mL) of the metal complex of quaternized N-(propyl) derivative of low-molecular chitosan with 53% substitution and 1.3% copper ions proved efficient against *F. oxysporum*, one of ten most common fungal plant pathogens. Water-soluble quaternized N-(propyl) chitosan derivatives with 40–58% degree of substitution were synthesized using glycidyltrimethylammonium chloride under optimally adjusted conditions. Metal complexes of the chitosan derivative with 53% degree of substitution with Cu(II) ions were obtained by dialysis. The quantity of copper ions in the metal complexes was determined by atomic emission spectrometry. The structure of chitosan derivatives was confirmed by spectral analysis (IR, ^{1}H NMR).

Keywords: chitosan, antifungal activity of chitosan, alkylated quaternized chitosan derivatives, chitosan metal complexes

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The search for and the development of new efficacious antifungal compounds is a highly important task due to the potential hazard that various species of fungi may represent in the agricultural sphere and in the field of healthcare. Various species of fungi damage agricultural plants, decreasing their productivity, cause spoilage of harvested crops, and may contaminate plant products with mycotoxins (Kulikov et al., 2006). Moreover, micromycete fungi are among the most common sources of allergens in the environment. The incidence of mycogenic allergy may vary from 6 to 24% in the general population and up to 44% in patients with atopic pathology (Khaldeeva et al., 2011); about 25% of bronchial asthma patients are sensitized to mold micromycetes (Mari et al., 2003). The yeasts of the genus *Candida* are among the most common agents causing deep and superficial chronic forms of diseases (Lisovskaya et al., 2016).

To decrease the burden on the ecological state of the environment, which is caused by the application of various pesticides, including synthetic fungicides, at present a fresh impetus has been given to active development and production of new fungicides based on biological compounds. Development of the fungicides based on chitosan, a natural polyaminosaccharide, as well as on chitosan-based derivatives and composites, is considered one of the promising avenues (Seyfarth et al., 2008; Rahman et al., 2014). The antifungal properties of chitosan are determined by its polycationic characteristics. The molecular mass and the degree of deacetylation of chitosan also influence the antifungal effect (Kulikov et al., 2009 and Rahman et al., 2015).

The presence of numerous amino groups in the chitosan polymer chain makes it possible to obtain chitosan-based derivatives with improved physicochemical characteristics, e.g., with higher solubility and biological activity (Il'ina et al., 2008). Chitosan functionalization is usually carried out by the amino group at C2 atom, as well as by the hydroxyl groups at C6 and C3 atoms of the glucosamine residue.

Obtaining chitosan derivatives containing quaternary nitrogen atoms is one of the ways of increasing the biocide activity of chitosan. Quaternized N-alkylated and arylated derivatives of high-molecular chitosan (700 kDa) have a considerably higher inhibitory activity against such plant pathogens as *Botrytis cinerea* and *Colletotrichum lagenarium* (Guo et al., 2007). Quaternized N-(propyl)- and (pentyl)-trimethylammonium chitosan bromide (20–32 kDa)